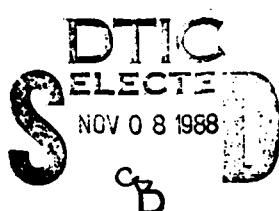


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## Tracheal pressure and impedance as determinants of gas exchange during high frequency ventilation

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**Abstract.** This work explores the use of catheter pressure transducers to measure time averaged, mean squared pressure (MSP) in the trachea of anesthetized animals during high frequency ventilation using a prototype Emerson oscillator with a 25 ml stroke volume at 15 and 34 Hz. Tidal volume and MSP were varied by shunting a portion of the ventilator output for the study of the effect of driving pressure on ventilation. A given level of ventilation was accomplished at a lower driving pressure at the lower frequency. Both ventilation as assessed by a modified nitrogen washout procedure and gas exchange were related to MSP and oscillatory frequency by the substitution of  $MSP/Z^2$  for alveolar ventilation in the equations of Jaeger *et al.* (1984). The technique and equations describing it were validated by the prediction of impedance changes resulting from shifts in oscillatory frequency. The calculated impedances matched experimentally measured values found in dogs by other investigators. Catheter pressure transducers are thus shown to be a useful tool for quantifying high frequency ventilation when coupled with a knowledge of respiratory impedance. The technique offers advantages over existing techniques, the most notable being ease of use due to the catheters' exceptional frequency response.

Blood gases; High frequency oscillation (HFO); Nitrogen washout; Power spectra; Tracheal pressure

It is generally believed that the effectiveness of High Frequency Oscillation (HFO) as a means of mechanical ventilation is dependent on the magnitude of the oscillating air flow (or tidal volume) delivered to the trachea (Bohn *et al.*, 1980; Slutsky *et al.*, 1980). Devices currently used to measure these flows, pneumotachometers and body plethysmographs, have characteristics which limit their use with HFO (Jackson and Vinegar, 1979; Simon *et al.*, 1984; Weinmann *et al.*, 1984). We wished to examine an alternative technique for quantifying HFO using catheter pressure transducers.

The first use of pressure, or specifically the square of pressure to describe the effect of HFO on gas exchange (Clarke *et al.*, 1983), was followed by work (Jaeger *et al.*, 1984) in which the square of oscillatory tidal volume was related to gas exchange. Here we

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have derived equations relating the two techniques. The following relationship was obtained:

$$P_{aO_2} = P_{lO_2} - Z^2/(\omega \cdot p^2).$$

The derivation of this equation is described in the methods sections. The above equation and others similar to it were used to relate nitrogen washouts and blood gases in anesthetized dogs to the mean squared pressure (MSP) measured in the dogs' tracheas. We observed that MSP affects gas exchange in much the same manner as does alveolar ventilation during conventional ventilation.

### Materials and methods

Dogs (*Canis familiaris*) were given a preanesthetic drug (xylazine, 2.2 mg/kg, i.m.) then anesthetized with sodium pentobarbital (11 mg/kg, i.v.). Atropine was administered periodically throughout the experiment to minimize tracheal secretions, and anesthesia was maintained by bolus pentobarbital injections as needed to suppress spontaneous ventilation. The animals were placed in the supine position and intubated with a prototype 4 lumen endotracheal (ET) tube (National Catheter Co, Argyle, NY) (fig. 1). The three small lumens of the ET tube were used (1) for delivery of a  $10 \text{ L} \cdot \text{min}^{-1}$  bias flow to the distal tip of the ET tube, (2) for gas sampling from the tip, and (3) for cuff inflation. The  $10 \text{ L} \cdot \text{min}^{-1}$  bias flow was inadequate for supporting ventilation by itself.

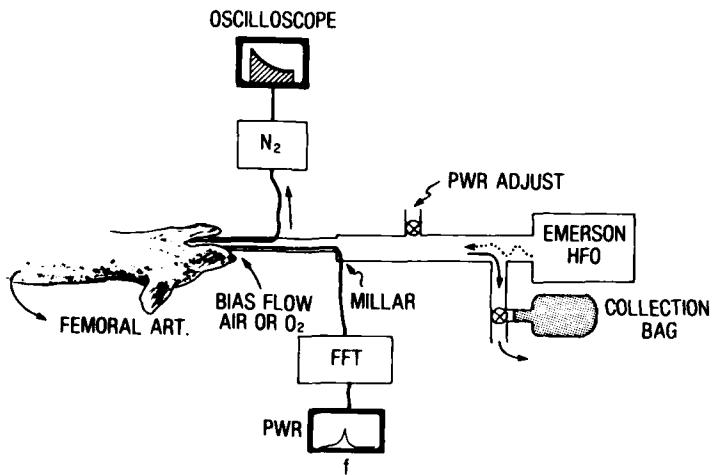


Fig. 1. Experimental setup. A 4-lumen endotracheal tube allowed both gas sampling from the distal tip of the tube and the delivery to the lower trachea of air or  $O_2$  at a flow of  $10 \text{ L} \cdot \text{min}^{-1}$ . The port used to vary MSP by shunting variable portions of the ventilator output is labeled PWR ADJUST (power adjust). The catheter pressure transducer is labeled MILLAR. The FFT output of the MSP power spectrum is referred to as PWR. Further details are provided in the text.

The large central lumen was connected to the high frequency oscillator and also served to carry the bias gas flow out of the lung.

Rectal temperature was maintained between 36 and 37°C with a heating pad. Cannulation of the femoral artery permitted continuous monitoring of arterial blood pressure and periodic analysis of arterial blood for  $\text{Pa}_{\text{O}_2}$ ,  $\text{Pa}_{\text{CO}_2}$ , and pH (Corning 165/2 blood gas analyzer, Corning Medical, Medfield, Mass).

An Emerson prototype diaphragm ventilator was used to provide sinusoidal flows with a 24–27 ml stroke volume at frequencies up to 34 Hz.

*Experimental techniques.* Pressure at the distal end of the ET tube was measured throughout the experiment by a piezo-resistive pressure transducer on the tip of a 5 French catheter (Model PC-350, Millar Instruments, Inc., Houston, TX). The frequency response of the transducer was specified by the manufacturer as being flat from 0 to 8000 Hz. The catheter was placed in the central lumen of the endotracheal tube near the distal tip and oriented to measure lateral pressures. A Nicolet 660A Fast Fourier Transform Analyzer (FFT), (Nicolet Scientific, Princeton, NJ) calculated average power spectra from the pressure signals. For sinusoidal inputs this involved a calculation of the mean squared pressure amplitude for a given frequency. RMS spectra, the time-average of the root of the mean signal, could also be obtained.

In preliminary studies, the response of the high frequency oscillator and pressure measurement system was checked in the following manner. Tidal volume of the Emerson oscillator was measured by a 104 L whole body plethysmograph, at frequencies from 12 to 34 Hz. The measured tidal volume was linear within 5% across the frequency range from 13 to 34 Hz. Total harmonic distortion was never more than 0.01%, indicating the spectral purity of the ventilator output and linearity of the plethysmograph response.

The frequency response of the catheter pressure transducer was checked by comparison with Brüel Kjaer condenser microphones (Type 4133 with a Cathode Follower Type 2615, Brüel Kjaer, Naerum, Denmark). Amplification was by a Brüel Kjaer Type 2606 Measuring Amplifier with a frequency response of 2–200 kHz. Probes were attached to the microphones allowing the measurement of lateral pressure within a long semi-rigid tube. The pressure amplitudes varied linearly throughout the frequency range of the ventilator.

Power spectra were calculated from the averaging of sixteen 4-sec pressure samples. Each sample consisted of 1024 discrete data points. The samples were filtered by low pass, anti-aliasing filters, allowing a useful frequency range of 0.13 to 100 Hz. Summation averaging with 50% redundancy was used, thus shortening the sampling interval.

The power of the second harmonic of the tracheal pressure recordings was at all times at least 12 db below the power at the fundamental frequency of the sinusoidal input from the ventilator. This insured that harmonic distortion of the tracheal pressure signal was less than 1%. If significant distortion occurred as a result of the catheter tip impinging on the tracheal wall, the catheter was withdrawn and reinserted until an appropriate signal obtained. Mean lateral pressures changed considerably between animals, depend-

ing on the orientation of the catheter transducer. However, catheter orientation was fixed throughout each experiment.

Nitrogen washouts were accomplished by using a  $10 \text{ L} \cdot \text{min}^{-1}$  flow of oxygen as a substitute for the usual bias flow of air. A Med Science 505 Nitralyzer (Med Science Electronics, St. Louis, MO) sampled gas continuously at  $3 \text{ ml} \cdot \text{min}^{-1}$  from the distal tip of the ET tube. The 90% response time for the Nitralyzer and associated catheter to a step input was 0.48 sec. The nitrogen concentration was recorded on a Nicolet Explorer II digital oscilloscope (Nicolet Scientific Corp, Northvale, NJ) and the digitized data transferred to a DEC N11/70 computer. The percent nitrogen was recorded every 0.4 sec, during which 67 ml of gas passed by the sampling port due to the bias flow. Time could thus be related to volume, and the amount of  $\text{N}_2$  washed out of the lungs was found from the areas under the  $\% \text{N}_2$ -volume curve (fig. 2). The greater the applied MSP, the greater was the area under the truncated washout curve and the volumetric washout of  $\text{N}_2$ .

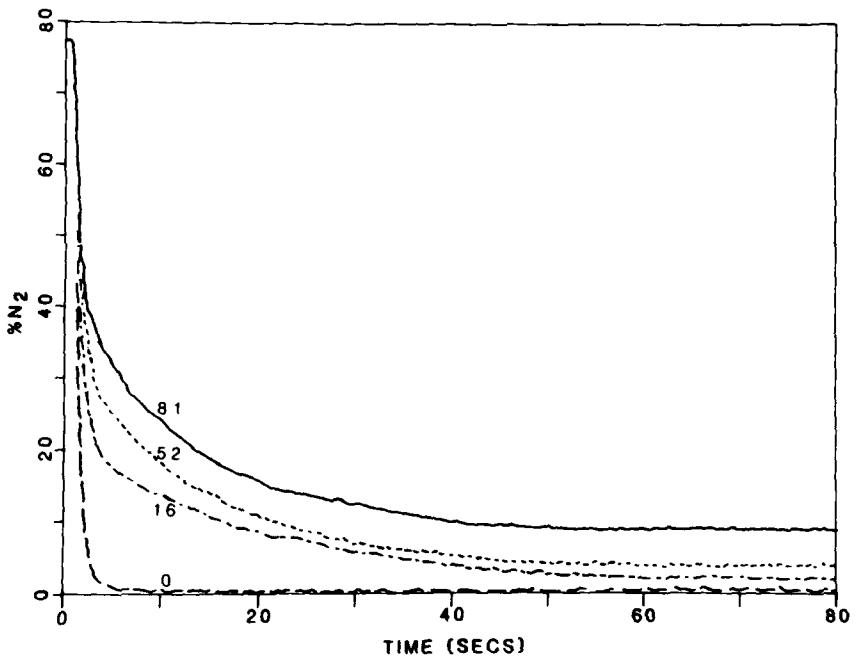


Fig. 2. The percentage of tracheal  $\text{N}_2$  vs time (sec) for various tracheal pressures (MSPs) as  $\text{O}_2$  washes in during HFO. Increasing areas beneath the truncated washout curves correspond to increasing amounts of  $\text{N}_2$  removed from the lung. MSP measured in the lower trachea in  $\text{cm H}_2\text{O}$  decreased from the top to the bottom curve.

Throughout this study, pressure at the distal trachea was varied by bleeding a portion of the output of the ventilator through a port upstream of the endotracheal tube. The open port could in principle allow room air into the system during nitrogen washouts. To test this possibility, we oscillated a Vent-aid lung model (Michigan Instruments Inc., Grand Rapids) with the MSP adjusting port surrounded with 100%  $\text{CO}_2$ .  $\text{CO}_2$  was

detected at the exit of the high impedance tube during oscillation. However,  $\text{CO}_2$  was never detected either within the model lung or at the distal tip of the ET tube regardless of the applied MSP or frequency. The conclusion was that  $\text{N}_2$  washouts were not contaminated by room air, most probably due to the  $10 \text{ L} \cdot \text{min}^{-1}$  flow of oxygen up the central lumen of the endotracheal tube.

*Experimental protocol.* One study included the dependence of tracheal nitrogen concentration upon Emerson ventilator frequency and MSP during washouts with  $\text{O}_2$ . Washouts were performed at 15 and 34 Hz in six 10 kg animals. The MSP adjusting port was allowed to shunt varying portions of the applied oscillations, thus reducing the measured tracheal MSP as desired. The gas supplying the bias flow was then switched to oxygen and the ensuing washout was recorded. For each animal an average of 6 washouts at varying MSPs was performed. The washouts were terminated after 2.5 min to limit hypoxia during low applied MSPs.

A single exponential equation was used as an empirical model to describe the volume (in ml) of nitrogen washed out in 2.5 min.

$$V_{\text{N}_2} = A_{\text{N}_2} \left(1 - e^{-\frac{\text{MSP}}{B_{\text{N}_2}}}\right). \quad (1)$$

Other work involved analyses of blood gases in samples obtained by femoral artery cannulation. For each of 5 animals (body mass =  $9.2 \pm 3.0 \text{ kg}$ , mean  $\pm 1 \text{ SD}$ ) a driving frequency for the ventilator was determined which provided normal ventilation and blood gas values. From this control state the oscillator frequency was changed in random order between 34 and 15 Hz. MSP was varied 6 times on the average at both 15 and 34 Hz by changing shunt size. Arterial blood samples were drawn in 1 ml heparinized glass syringes at 3 and 6 min after the frequency and MSP changes. Each test run was followed by a 10 minute period of control ventilation without sighs, after which an additional blood sample was drawn to confirm return to the control state. On the average, 48 blood samples were drawn per animal, with saline replacement. Time averaged tracheal MSP was computed by the FFT analyzer during the first minute of each experimental exposure.

The relationship between  $\text{Pa}_{\text{O}_2}$  and MSP was modeled by the following empirical equation based on the general form of the alveolar air equation with MSP being substituted for ventilation.

$$\text{Pa}_{\text{O}_2} = A_{\text{O}_2} - (B_{\text{O}_2}/\text{MSP}). \quad (2)$$

$\text{Pa}_{\text{CO}_2}$  was expressed by a related empirical equation:

$$\text{Pa}_{\text{CO}_2} = A_{\text{CO}_2} + (B_{\text{CO}_2}/\text{MSP}). \quad (3)$$

*Statistics.* Parameters A and B were obtained for each experimental condition by fitting either the nitrogen washout or blood gas data to their respective models by the

least squares technique (Marquardt, 1963). Analysis of variance was used to test the differences between parameters for the blood gas studies with significance being determined by the F-test for  $P < 0.05$ . For nitrogen washouts, the non-parametric sign test was used to compare fitted parameters.

*Rationale.* The rationale for the use of MSP and eqs. (1-3) are based upon our derivation using the alveolar air equation as follows:

$$P_{AO_2} = P_{I_{O_2}} - P_{ACO_2}/R$$

and

$$P_{ACO_2} = K \cdot \dot{V}_{CO_2}/\dot{V}_A.$$

Combining,  $P_{AO_2} = P_{I_{O_2}} - [(\dot{V}_{CO_2})K/(R \cdot \dot{V}_A)]$  where the usual definitions apply; *e.g.*  $P_{AO_2}$  equals alveolar, and presumably arterial  $O_2$  tension,  $P_{I_{O_2}}$  is inspired  $O_2$  tension,  $P_{ACO_2}$  is alveolar  $CO_2$ , and  $R$  is the respiratory exchange ratio.  $\dot{V}_{CO_2}$  is  $CO_2$  output and  $\dot{V}_A$  is alveolar ventilation.  $K$  is a constant.

In conventional ventilation,  $\dot{V}_A = f \cdot (V_T - V_D)$  where  $f$  is frequency in Hz,  $V_T$  is tidal volume, and  $V_D$  is dead space. For HFO, however, we substitute from the literature  $\dot{V}_A = k \cdot \omega \cdot V_T^2/V_D$  (Jaeger *et al.*, 1984), where  $\omega$  is angular frequency (radians · sec<sup>-1</sup>), and  $V_T$  is the stroke or 'tidal volume' of the HFO ventilator.

If the lung volume distal to the sinusoidal forcing pressure  $P$  responds as the solution to a linear differential equation then RMS volume about a mean volume will be proportional to the RMS pressure about the mean forcing pressure. The proportionality constant will be the reciprocal of a polynomial impedance ( $Z$ ) at the forcing frequency.

$$VRMS = (MSP)^{0.5}/Z.$$

Recalling that  $V_T$  will be proportional to RMS volume ( $V_T = K \cdot VRMS$ ), then we may substitute into the formula of Jaeger and Kurzweg to obtain an approximation to  $\dot{V}_A$ .

$$\dot{V}_A = (K \cdot \omega/V_D \cdot Z^2) \cdot MSP \quad (4)$$

therefore  $P_{AO_2} = P_{I_{O_2}} - (\dot{V}_{CO_2} \cdot K \cdot V_D \cdot Z^2)/(R \cdot k \cdot \omega \cdot MSP)$ .

Letting  $A = P_{I_{O_2}}$ , and assuming that  $\dot{V}_{CO_2}$ ,  $V_D$ , and  $R$  are constant,

$$P_{AO_2} = A - (K' \cdot Z^2)/(\omega \cdot MSP).$$

With frequency fixed, this further simplified to

$$P_{AO_2} = A - B/MSP, \text{ or eq. (2).}$$

Since the B parameters in eqs. (1-3) have common dimensions of reciprocal MSP units, and with the justification of eq. (4), the B parameters were used to solve for the ratios of estimated impedance at 34 Hz ( $Z_{34}$ ) and 15 Hz ( $Z_{15}$ ).  $Z' = Z_{34}/Z_{15} = (2.267 \cdot B_{34}/B_{15})^{0.5}$ . This relationship was derived from the fact that  $B_{34} = (K' \cdot Z_{34}^2)/\omega_{34}$  and  $\omega_{34} = 2 \cdot \pi \cdot 34$  Hz.

## Results

**MSP vs nitrogen flux.** The area under the  $\%N_2$  vs volume (time) curve increased curvilinearly with increasing MSP (fig. 3). As shown in table 1, all animals had a significantly larger B parameter (eq. (1)) at 34 Hz than at 15 Hz. When tested by the

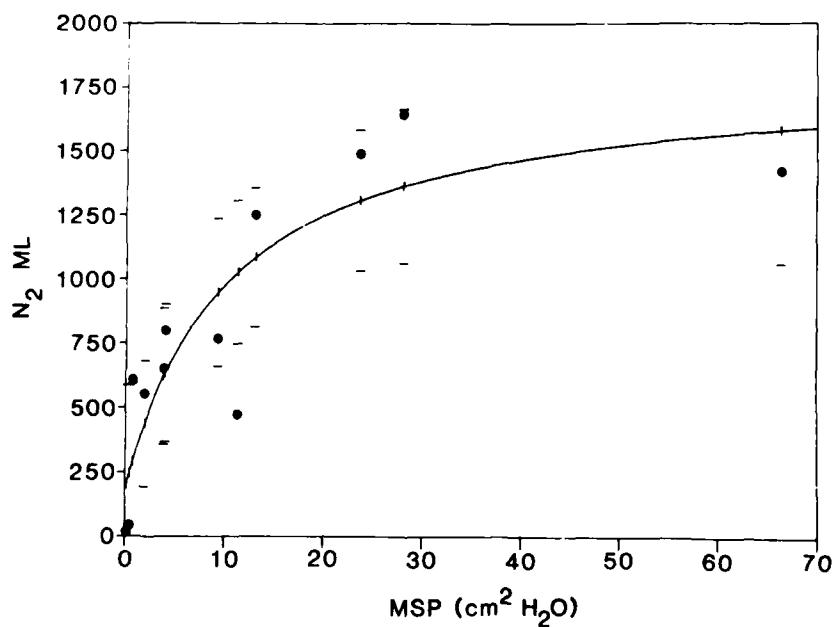


Fig. 3. Volume of  $N_2$  in ml removed during an 80 sec washout vs MSP at 34 Hz. The data for one dog are given, along with the best fit to the data based on eq. (1); horizontal bars associated with each data point mark the 95% confidence limits for the regression.

sign test this difference was statistically significant. The B parameter for the 34 Hz data was  $3.4 \pm 0.8$  (mean  $\pm$  1 SE) times greater than the B parameter for the 15 Hz data.

**Gas exchange.** As with other high frequency ventilators, higher frequencies resulted in better gas exchange when the full, non-shunted, output of the ventilator was applied to the animals, due presumably to the higher flow rates. When frequency was fixed,  $Pa_{O_2}$  increased curvilinearly toward a plateau as MSP was increased by bleeding less gas through the shunt (fig. 4). It was assumed that the plateau for  $Pa_{O_2}$  at infinite MSP at

TABLE 1

Parameters for the fit of the following equation to the nitrogen washout data in 6 dogs:

$$V_{N_2} = A \left[ 1 - e^{-\frac{MSP\%}{B}} \right].$$

The ml of nitrogen washed out of the lung was dependent upon MSP%, the percentage of the mean MSP for a given animal as MSP was varied via the power adjusting port or shunt. The asymptote (A) is assumed to be common to both data sets. B was allowed to vary with frequency. Mean estimated values  $\pm$  the SE of the estimate for parameters A and B are given. Z' is the ratio of estimated impedance at 34 and 15 Hz. The values at the bottom of each column are the means for that column.

Asymptote (mean $\pm$ SE)	B34	B15	B34/B15	Z'
1464 $\pm$ 179	435 $\pm$ 147	61 $\pm$ 138	7.1	4.0
739 $\pm$ 26	79 $\pm$ 24	41 $\pm$ 27	1.9	2.1
1584 $\pm$ 111	199 $\pm$ 49	63 $\pm$ 46	3.2	2.7
1026 $\pm$ 77	24 $\pm$ 9	7 $\pm$ 10	3.4	2.8
989 $\pm$ 44	37 $\pm$ 9	22 $\pm$ 11	1.7	2.0
1444 $\pm$ 209	400 $\pm$ 121	144 $\pm$ 102	2.8	2.5
	196	56	3.4	2.7

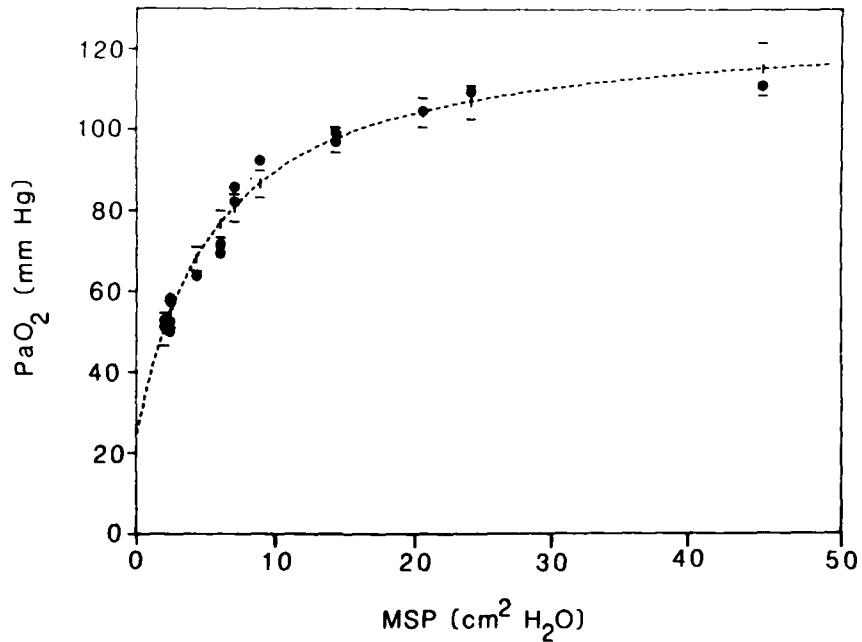


Fig. 4. Arterial  $Pa_{O_2}$  in one animal after the application of various MSPs to the trachea at 34 Hz. The best estimate (vertical dashed line) and 95% confidence limits for the estimate are also given.

34 Hz was the same as at 15 Hz. This assumption seems reasonable but in any case was necessary since the maximum MSPs generated at 15 Hz were not large enough to give a clear plateau. The values for the estimated parameters are given in table 2. Due presumably to geometrical factors, raw MSPs varied greatly between animals. To minimize the effect of this variation, individual MSPs for a given experiment were expressed as a percentage of their mean; an MSP equal to the mean was given a value of 100. The model fits were then made from this normalized data.

TABLE 2  
Parameters for the fit of the following equation to  $\text{Pa}_{\text{O}_2}$  vs MSP.

$$\text{Pa}_{\text{O}_2} = A - (B \text{ MSP}^{\circ}\text{o}).$$

The arterial  $\text{Pa}_{\text{O}_2}$  was dependent upon  $\text{MSP}^{\circ}\text{o}$ , the percentage of the mean MSP for a given animal. The asymptote (A, maximum  $\text{Pa}_{\text{O}_2}$ ) was assumed to be common to both data sets. B was allowed to vary with frequency. Mean estimated values  $\pm$  the SE of the estimate for parameters A and B are given. Z' is the ratio of estimated impedance at 34 and 15 Hz. The values at the bottom of each column are the means for that column.

Animal no.	$A = \text{Pa}_{\text{O}_2} \text{max}$	B34 B15	B15	Z'
1	$90 \pm 2$	$4.4 \pm 0.5$	$18.6 \pm 2.6$	3.2
2	$96 \pm 3$	$4.1 \pm 0.6$	$81.9 \pm 18.6$	3.1
3	$94 \pm 3$	$2.0 \pm 0.3$	$38.1 \pm 6.2$	2.1
4	$106 \pm 3$	$3.2 \pm 3$	$13.7 \pm 14.1$	2.7
5	$105 \pm 3$	$3.3 \pm 0.7$	$48.9 \pm 12.8$	2.7
	98	3.4	40.2	2.8

TABLE 3  
Parameters for the fit of the  $\text{Pa}_{\text{CO}_2}$  vs MSP data to the equation:

$$\text{Pa}_{\text{CO}_2} = A + (B/\text{MSP}^{\circ}\text{o}).$$

$\text{MSP}^{\circ}\text{o}$  was the percentage of the mean MSP for a given animal as MSP was varied. The asymptote (A, minimum  $\text{Pa}_{\text{CO}_2}$ ) was assumed to be common to both data sets. B was allowed to vary with frequency. Mean estimated values  $\pm$  the SE of the estimate for parameters A and B are given. Z' is the ratio of estimated impedance at 34 and 15 Hz. The values at the bottom of each column are the means for that column.

Animal no.	$A = \text{Pa}_{\text{CO}_2} \text{min}$	B34 B15	B15	Z'
1	$33 \pm 2$	$5.0 \pm 1.3$	$5.8 \pm 1.9$	3.4
2	$33 \pm 1$	$3.1 \pm 0.7$	$19.9 \pm 6.6$	2.7
3	$25 \pm 1$	$1.6 \pm 0.2$	$17.3 \pm 2.2$	1.9
4	$21 \pm 1$	$0.8 \pm 0.2$	$16.6 \pm 4.5$	1.4
5	$22 \pm 1$	$4.4 \pm 2.0$	$6.7 \pm 3.4$	3.2
	27	3.0	13.3	2.5

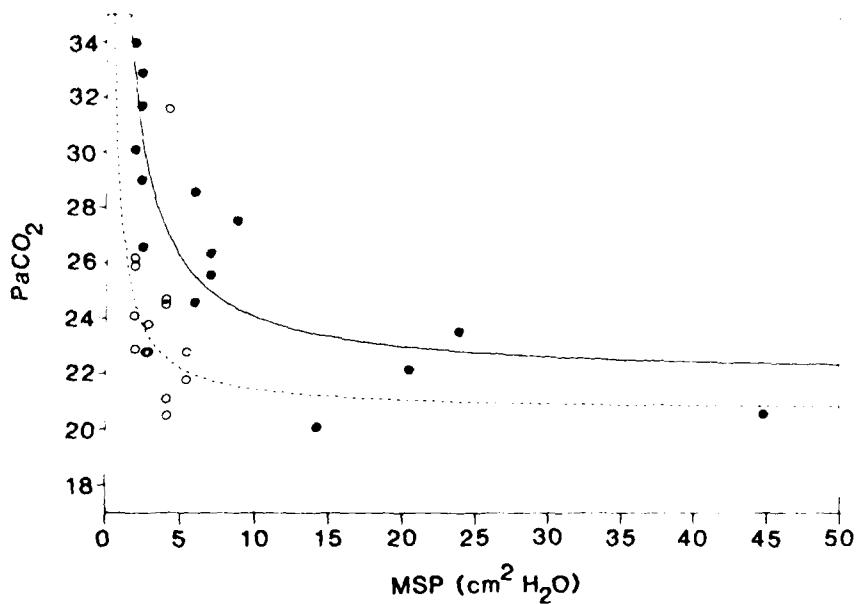


Fig. 5. (a) Arterial  $\text{PaCO}_2$  vs MSP. The blood samples were the same as those in Fig. 4. Open circles = 15 Hz, closed circles = 34 Hz.

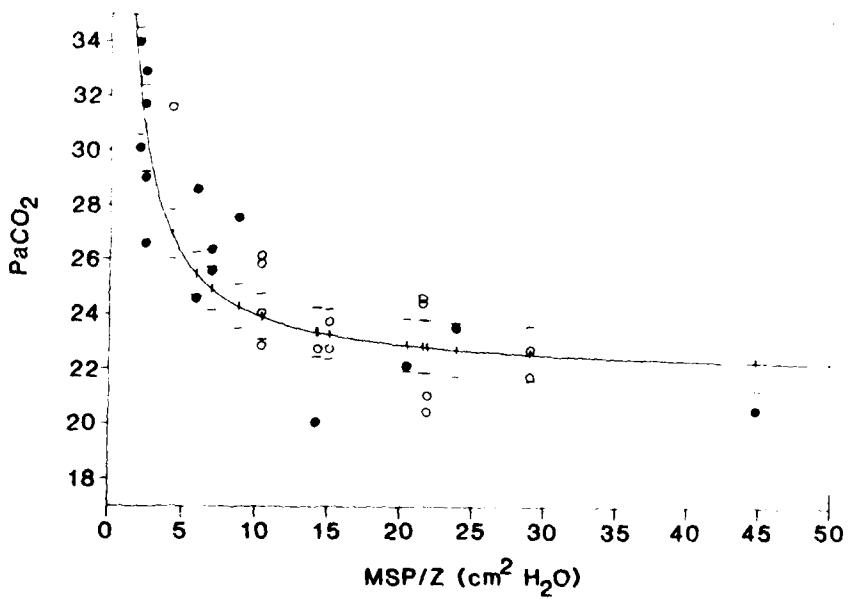


Fig. 5. (b) The result of normalizing  $\text{PaCO}_2$  by the computed impedance at 15 and 34 Hz. Open circles = 15 Hz, closed circles = 34 Hz. This suggests that the previously identifiable differences between the two curves are attributable to the relative impedances at those frequencies.

All animals demonstrated significant differences between the blood gas data at 34 Hz and 15 Hz as tested by analysis of variance (table 2). Specifically,  $\text{Pa}_{\text{O}_2}$  rose more rapidly with increasing MSP at 15 Hz than it did at 34 Hz. The mean for the ratios of B at 34 Hz vs B at 15 Hz for the same animal was on the average equal to  $3.4 \pm 0.4$  (mean  $\pm$  1 SE). The estimated maximum  $\text{P}_{\text{O}_2}$  for all 5 animals was  $98 \pm 3$  (SE) mm Hg.

As MSP was increased  $\text{P}_{\text{CO}_2}$  dropped faster at 15 Hz than it did at 34 Hz (fig. 5a). When the model in eq. (3) was applied, 4 out of 5 curves at 15 Hz were significantly different as determined by analysis of variance from those obtained at 34 Hz in the same animal (table 3).

**Impedance.** For all cases, calculated impedance at 34 Hz was considerably greater than impedance at 15 Hz. The mean ratio of impedance ( $Z'$ ) based on the  $\text{Pa}_{\text{O}_2}$  measurements was  $2.8 \pm 0.4$  (mean  $\pm$  SE). That is to say, the estimated impedance at 34 Hz was 2.8 times greater than 15 Hz.  $Z'$  for  $\text{N}_2$  was  $2.7 \pm 0.7$ .  $Z'$  calculated from the  $\text{CO}_2$  data was  $2.5 \pm 0.8$ . When  $Z' \text{N}_2$ ,  $Z' \text{O}_2$ , and  $Z' \text{CO}_2$  was averaged, the total  $Z'(\text{tot}) = 2.6 \pm 0.2$  (mean  $\pm$  SE,  $n = 16$ , range = 1.4–4.0). The  $\text{Pa}_{\text{CO}_2}$  data from one experiment are plotted against  $\text{MSP}/Z'$  in fig. 5b. For the data shown,  $Z'$  was equal to 2.9. Normalization by  $Z'$  resulted in a single curve rather than dual curves.

**MSP.** One data set contained enough data (fig. 4) to allow estimation of the exponent of MSP, which has throughout been assumed to be 1.0. The estimated exponent was

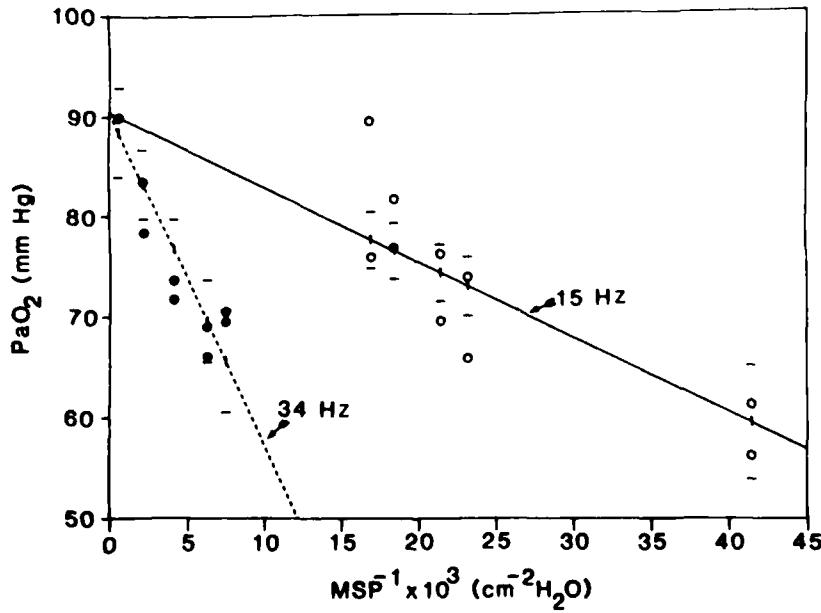


Fig. 6.  $\text{Pa}_{\text{O}_2}$  at 34 and 15 Hz in one animal as a function of the reciprocal of MSP. The solid and dotted lines represent the linear regression for this data. Horizontal bars represent 95% confidence limits on the regression. See text for details.

somewhat dependent on the y-intercept, the  $\text{Pa}_{\text{O}_2}$  after 6 min of apnea (MSP = 0). Since this measurement was not made, for the safety of the animal, some assumptions were necessary. When the apneic  $\text{Pa}_{\text{O}_2}$  was assumed to be zero, the exponent of MSP was estimated to be  $0.93 \pm 0.06$  (mean  $\pm$  SE of the estimate). If instead the intercept was believed to be 10 mm Hg, then the exponent was estimated as  $0.99 \pm 0.06$ . With a  $\text{Pa}_{\text{O}_2}$  of 20 mm Hg, the exponent of MSP would be  $1.08 \pm 0.07$ .

When  $\text{Pa}_{\text{O}_2}$  and  $\text{Pa}_{\text{CO}_2}$  were plotted against  $1/\text{MSP}$  approximately linear relationships obtained (fig. 6). For the  $\text{Pa}_{\text{O}_2}$  data, a correlation coefficient of  $0.90 \pm 0.06$  (mean  $\pm$  SD) was found for the 34 Hz data and  $0.78 \pm 0.6$  for the 15 Hz data.

## Discussion

*Alternative techniques.* Catheter pressure transducers were used in this study in an effort to avoid some of the limitations of alternative techniques of measuring flows generated during high frequency oscillation. These techniques are (1) the measurement of ventilator stroke volume, (2) flow measurement with a pneumotachograph, (3) volume changes measured by a plethysmograph.

Early investigators using piston type high frequency ventilators (Bohn *et al.*, 1980) related the physiological effect of HFV to the stroke volume of the ventilator. However, Watson *et al.* (1984) found that errors in relating stroke volume to delivered tidal volume were introduced by both leaks within the ventilator and by gas compression. According to Watson *et al.*, for a tidal volume of 25 ml, errors of 25% could result.

Ultimately, the effect of HFO is dependent on flow. Pneumotachometers, common flow measuring devices, typically demonstrate a linear frequency responses (Jackson and Vinegar, 1979), complicating their use during HFO. In addition, a portion of the gas measured by a pneumotachometer is shunted into the expansion of upper airways (Gavriely *et al.*, 1985), thus not all the gas measured by pneumotachometers during HFO contributes to ventilation. The magnitude of the overestimation of alveolar ventilation depends on the impedance of airways peripheral to the carina.

Pressure plethysmographs have been used to estimate tidal volumes delivered during HFO, but these devices are reported to have a relatively low frequency response (25 Hz, Weinmann *et al.*, 1983; Simon *et al.*, 1984) due to distortions generated within the plethysmographs. Indeed, there is a trade-off between the small plethysmograph size needed for good amplitude response and large size needed to minimize nonlinearity caused by harmonic distortion. This latter result can be derived from the Fourier transform of equations relating box pressure to sinusoidal forcing functions (G. Atlas, personal communication). The plethysmograph used in this study, with a volume equal to 104 L, had excellent response and signal quality up to 37 Hz. However, its use in HFV studies with instrumented animals was still highly cumbersome.

*Tracheal pressure.* This work has demonstrated that tracheal pressure can be used to monitor ventilation during HFO just as effectively as can flow measuring devices, with

arterial blood gases curvilinearly related to MSP just as they are related to ventilation in conventional ventilation. Millar catheters have the advantages of small size, to fit unobtrusively within endotracheal tubes and large airways, and of inherent linearity over an extremely wide frequency range. The only disadvantage is that pressure measurements must be coupled with impedance information to allow estimates of flows and tidal volumes. Lastly, in spite of the superficial appearance that ventilation is improved at higher frequencies, when compared on an equal MSP basis 34 Hz does not provide improved gas exchange over 15 Hz.

**Squared pressure.** The equation published by Jaeger *et al.* (1984) and used in our above derivation is similar with respect to the  $VT^2$  term to the equation for  $\text{CO}_2$  transport during HFO developed independently by Mitzner *et al.* (1983). The results of Jaeger *et al.* (1984) were furthermore similar to those of Kamm *et al.* (1982). A number of researchers who originally espoused a linear relationship between  $\dot{V}_{\text{CO}_2}$  and flow ( $VT \cdot f$ , Slutsky *et al.*, 1980) now recognize that  $VT$  exerts its own independent effect on gas transport (Slutsky *et al.*, 1981).

Although we have made heavy use of  $\text{MSP}^{1.0}$ , based on suggestions from the literature, this work was not designed to test the correctness of that assumption. Obviously, the square root of MSP or time averaged pressure would have been a reasonable alternative. One data set, however, contained enough data (fig. 4) to allow estimation of the exponent of MSP. The additional constraint of a positive y-intercept was first needed, however. This constraint was not unreasonable since the effects of cardiac motion and bias flow (Lehnert *et al.*, 1982) can induce some ventilation in the absence of all respiratory motion. The mean estimate for the exponent of MSP in one animal assuming y-intercepts of 0–20 mm Hg was  $1.00 \pm 0.07$  (mean  $\pm$  SE of the estimate). This analysis therefore provides tentative support for the use of  $\text{MSP}^{1.0}$  in the foregoing equations.

**Bias flow effects.** The present model predicts that at infinite MSP,  $\text{Pa}_{\text{CO}_2}$  will be zero, and therefore (A) in eq. (3) must be zero. However,  $\text{Pa}_{\text{CO}_2}$  seemed to plateau at levels substantially above zero (table 3). This elevation of the plateau may be due to our inability to supply an infinite bias flow. Solway *et al.* (1985) used the following equation to describe the effect of bias flow rate on high frequency ventilation:

$$\dot{M}_{\text{CO}_2} = \text{Pa}_{\text{CO}_2} / [1/(\dot{V}_b \cdot B) + 1/G]$$

where  $\dot{M}_{\text{CO}_2}$  was  $\text{CO}_2$  flux in  $\text{ml STPD} \cdot \text{min}^{-1}$ , G was airway  $\text{CO}_2$  conductance with units of  $\text{ml STPD} \cdot \text{Torr} \cdot \text{min}^{-1}$ ,  $\dot{V}_b$  was bias flow in  $\text{L} \cdot \text{min}^{-1}$ , and B was a temperature correction coefficient with units of  $\text{ml STPD} \cdot \text{L}^{-1} \cdot \text{Torr}^{-1}$ . For the non-steady state explored by these investigators,  $\text{Pa}_{\text{CO}_2}$  remained constant during the brief period of an experiment. In steady state conditions, however,  $\dot{M}_{\text{CO}_2}$  becomes equal to metabolic  $\text{CO}_2$  production, and  $\text{Pa}_{\text{CO}_2}$  varies. Rearranging:

$$\text{Pa}_{\text{CO}_2} (\text{steady state}) = \dot{M}_{\text{CO}_2} / (\dot{V}_b \cdot B) + \dot{M}_{\text{CO}_2} / G = A + B/G .$$

$G$  is a function of frequency and tidal volume (Fredberg, 1980), or in our case, a function of frequency and tracheal MSP when conductance is infinite,  $Pa_{CO_2}$  is an inverse function of bias flow rate, and approaches zero only as  $V_b$  approaches infinity. This equation has the form of eq. (3) with  $G$  proportional to MSP. According to Lehnert *et al.* (1982) and Rossing *et al.* (1984), bias flow may also affect  $B$  in eq. (3) by altering either dead space or delivered tidal volume. Details of this proposed interaction were not given.

Equation (3) can be modified to include the effects of bias flow:

$$Pa_{CO_2} = 1/(k_1 \cdot \dot{V}_b) + (k_2 \cdot \dot{V}_{CO_2} \cdot V_d \cdot Z^2)/R(k_3 \cdot \dot{V}_b \cdot \omega \cdot MSP).$$

An analogous equation can be derived for  $Pa_{O_2}$ , and for the same reason; in this study the  $O_2$  tension remained below the predicted maximum. The endotracheal tube position is also a factor, presumably influencing dead space,  $V_D$  (Rossing *et al.*, 1984). Since  $\dot{V}_b$  was held constant in this study, the above hypothesized equation could not be tested.

*Impedance ratios.* The ratios of impedance at 34 and 15 Hz (calculated from the ratios of  $B$  parameters) were consistent; they were similar whether obtained from the  $Pa_{CO_2}$ ,  $Pa_{O_2}$ , or  $N_2$  washout measurements. They furthermore agreed with other directly measured values of impedance. Watson *et al.* (1984) measured impedance in 11 dogs at frequencies up to 40 Hz. Their plot of impedance amplitude *vs* frequency for all 11 dogs showed that an increase of frequency from 15 to 34 Hz increased impedance approximately 2.8 times. This compares well with our calculated value of 2.7. This agreement between Watson's data and our own suggests that the equations used in this work are basically correct and that a lower impedance may be responsible for the efficiency of the 15 Hz oscillation.

We have shown that it is possible to calculate impedance from blood gas or nitrogen washout data. Conversely, with a knowledge of impedance, ventilation can be predicted during HFO using the MSP relationship developed here. Referring to the linear relationship between blood gas tensions and the reciprocal of MSP we remember that the slope of  $Pa_{O_2}$  *vs*  $1/MSP$  is predicted to be  $Z^2/\omega$ . Substituting data for  $Z$  from Watson *et al.* (1984), the slope for 34 Hz data should be approximately 3.5 times the slope of 15 Hz data. In table 2 that ratio of slopes is seen to average 3.4. The  $Pa_{CO_2}$  data (table 3), though more variable, had an average slope ratio of 3.0. So knowing the effects of pressure on gas exchange at one frequency for a given animal, we find that predictions of blood gas tension for another frequency agree well with our experimentally determined mean values of  $Pa_{O_2}$  and  $Pa_{CO_2}$ . Further exploration of the predictive value of this approach, however, will require more animals than were used here.

*In summary*, we have used the time averaged square of tracheal pressure to describe the effect of HFO on gas exchange. This method, first described by Clarke *et al.* (1983), has similarities to the methods of Jaeger *et al.* (1984), where the square of oscillatory tidal volume was related to gas exchange. Here we have derived equations relating the two techniques. This was done by the calculation of impedance in a first order linear

model of the respiratory system, and by substituting pressure and impedance terms for flow and its integral, tidal volume, in the alveolar air equation. The new equations fit the experimental data well, predicting that blood gases would follow a curvilinear course to a plateau. The frequency dependence of the curves was explained solely by differences in impedance, which matched impedance values in the literature. We suggest that the use of pressure, especially pressures that can be measured through a major portion of the bronchial tree, simplifies the monitoring of HFO.

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